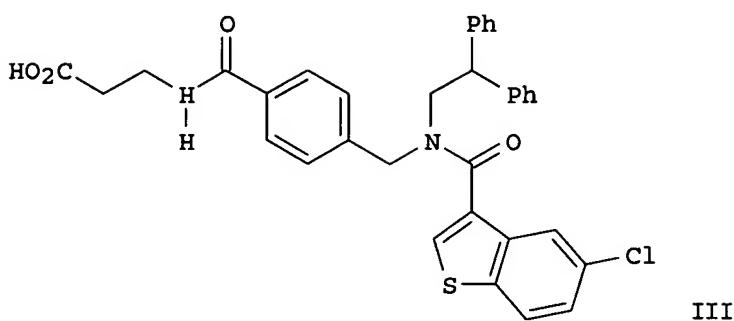
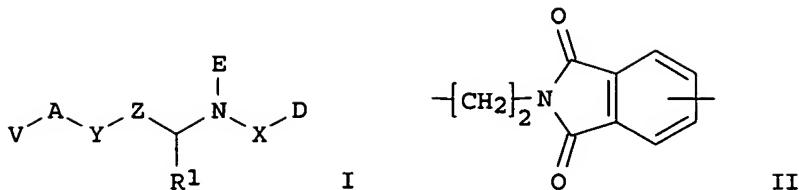


L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2000:824211 CAPLUS  
 DOCUMENT NUMBER: 134:4764  
 TITLE: Preparation of 3-(benzoylamino)propionic acid derivatives as glucagon antagonists/inverse agonists  
 INVENTOR(S): Ling, Anthony; Plewe, Michael Bruno; Truesdale, Larry Kenneth; Lau, Jesper; Madsen, Peter; Sams, Christian; Behrens, Carsten; Vagner, Josef; Christensen, Inge Thoger; Lundt, Behrend Frederik; Sidelmann, Ulla Grove; Thogersen, Henning  
 PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.; Agouron Pharmaceuticals, Inc.  
 SOURCE: PCT Int. Appl., 564 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000069810	A1	20001123	WO 2000-DK264	20000516
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6503949	B1	20000516	US 2000-572553	20000516
CA 2373892	AA	20001123	CA 2000-2373892	20000516
EP 1183229	A1	20020306	EP 2000-926725	20000516
EP 1183229	B1	20051026		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000010651	A	20020319	BR 2000-10651	20000516
JP 2002544254	T2	20021224	JP 2000-618228	20000516
AT 307798	E	20051115	AT 2000-926725	20000516
ZA 2001008560	A	20020613	ZA 2001-8560	20011018
NO 2001005607	A	20020117	NO 2001-5607	20011116
US 2003220350	A1	20031127	US 2002-233851	20020830
US 6875760	B2	20050405		
US 2005203108	A1	20050915	US 2004-980199	20041103
PRIORITY APPLN. INFO.:			DK 1999-684	A 19990517
			DK 2000-478	A 20000321
			US 1999-134415P	P 19990517
			US 2000-191685P	P 20000323
			US 2000-572553	A3 20000516
			WO 2000-DK264	W 20000516
			US 2002-233851	A3 20020830

OTHER SOURCE(S): MARPAT 134:4764  
 GI



**AB** The title compds. [I; V = CO<sub>2</sub>R<sub>2</sub>, CONR<sub>2</sub>R<sub>3</sub>, CONR<sub>2</sub>OR<sub>3</sub>, etc. (wherein R<sub>2</sub>, R<sub>3</sub> = H, alkyl); A = (CH<sub>2</sub>)<sub>n</sub>(CR<sub>8</sub>R<sub>9</sub>)<sub>b</sub>NR<sub>7</sub>, (CR<sub>8</sub>R<sub>9</sub>)<sub>b</sub>(CH<sub>2</sub>)<sub>n</sub>NR<sub>7</sub>, (CR<sub>8</sub>R<sub>9</sub>)<sub>b</sub>(CH<sub>2</sub>)<sub>n</sub>, etc. (b = 0-1; n = 0-3; R<sub>7</sub> = H, alkyl, (cycloalkyl)alkyl; R<sub>8</sub>, R<sub>9</sub> = H, alkyl); Y = CO, SO<sub>2</sub>, O, a bond; Z = (un)substituted phenylene, divalent radical derived from 5-6 membered heteroarom. ring containing 1-2 heteroatoms selected from N, O and S; or AYZ together = II; R<sub>1</sub> = H, alkyl; X = CO(CR<sub>13</sub>R<sub>14</sub>)<sub>r</sub>(CH<sub>2</sub>)<sub>s</sub>, SO<sub>2</sub>(CR<sub>13</sub>R<sub>14</sub>)<sub>r</sub>(CH<sub>2</sub>)<sub>s</sub>, CO<sub>2</sub>(CR<sub>13</sub>R<sub>14</sub>)<sub>r</sub>(CH<sub>2</sub>)<sub>s</sub>, etc. (r = 0-1; s = 0-3; R<sub>13</sub>, R<sub>14</sub> = H, alkyl); D = (un)substituted Ph, pyridyl, cyclopropyl, etc.; E = (un)substituted quinolinyl, 2,5-dioxopiperidinyl, biphenylalkyl, etc.] which act to antagonize the action of the glucagon hormone on the glucagon receptor (data given), and therefore may be suitable for the treatment and/or prevention of any glucagon-mediated conditions and diseases such as hyperglycemia, Type 1 diabetes, Type 2 diabetes and obesity, were prepared and formulated. E.g., a multi-step solid phase synthesis of III was given. Compds. I are effective at 0.05-10 mg/kg/day.

**IT**

307983-19-3P 307983-20-6P 307984-25-4P  
 307984-84-5P 307984-85-6P 307984-86-7P  
 307985-00-8P 307985-16-6P 307985-74-6P  
 307986-43-2P 307986-44-3P 307986-45-4P  
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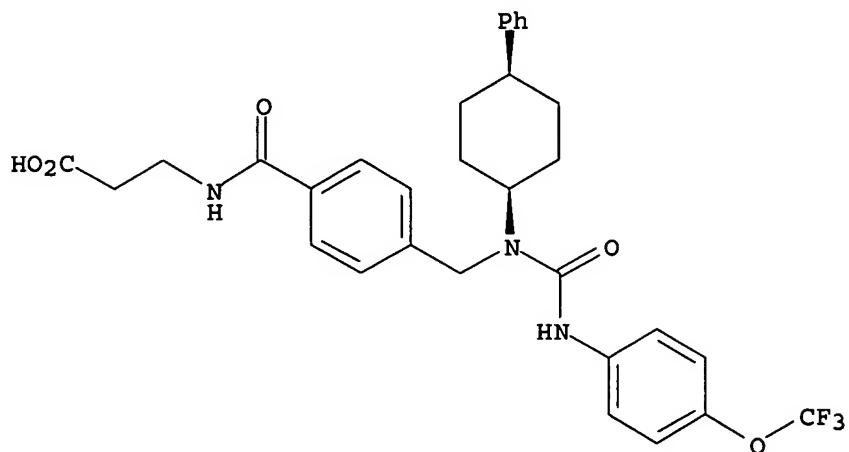
**RL:** BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of 3-(benzoylamino)propionic acid derivs. as glucagon antagonists/inverse agonists)

**RN** 307983-19-3 CAPLUS

**CN**  $\beta$ -Alanine, N-[4-[(cis-4-phenylcyclohexyl)[[[4-

(trifluoromethoxy)phenyl]amino]carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)

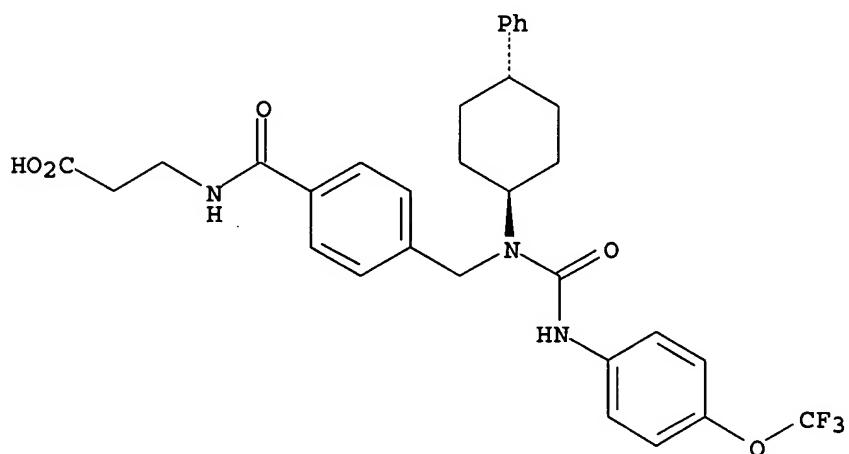
Relative stereochemistry.



RN 307983-20-6 CAPLUS

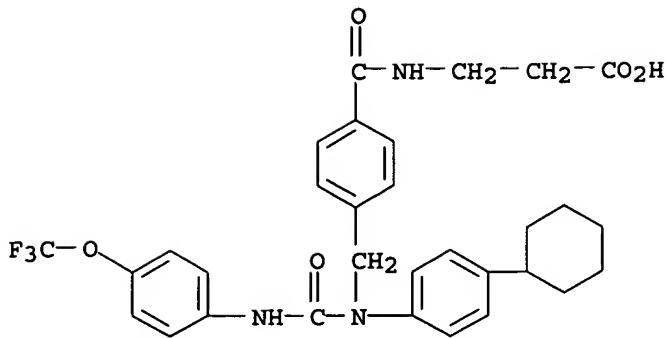
CN  $\beta$ -Alanine, N-[4-[(trans-4-phenylcyclohexyl)[[4-(trifluoromethoxy)phenyl]amino]carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

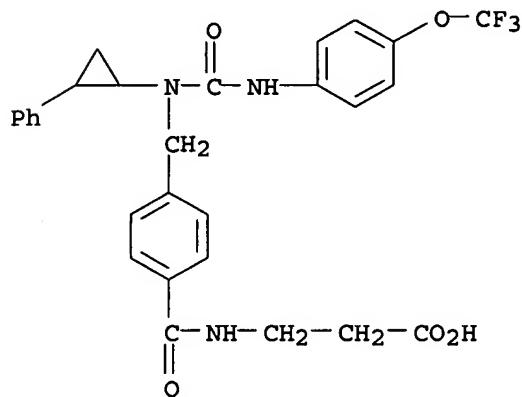


RN 307984-25-4 CAPLUS

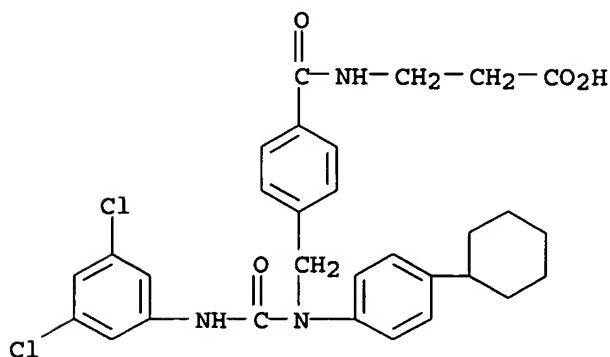
CN  $\beta$ -Alanine, N-[4-[(4-cyclohexylphenyl)[[4-(trifluoromethoxy)phenyl]amino]carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)



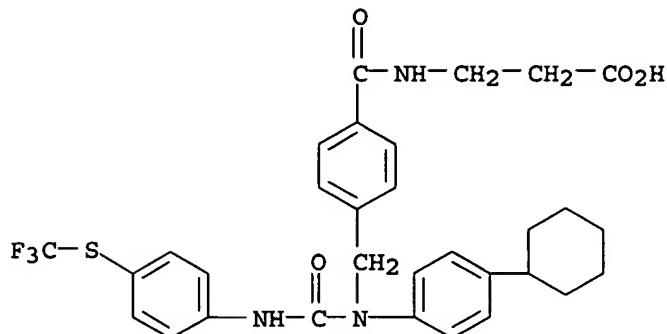
RN 307984-84-5 CAPLUS

CN  $\beta$ -Alanine, N-[4-[(2-phenylcyclopropyl)[[[(4-(trifluoromethoxy)phenyl]amino]carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)

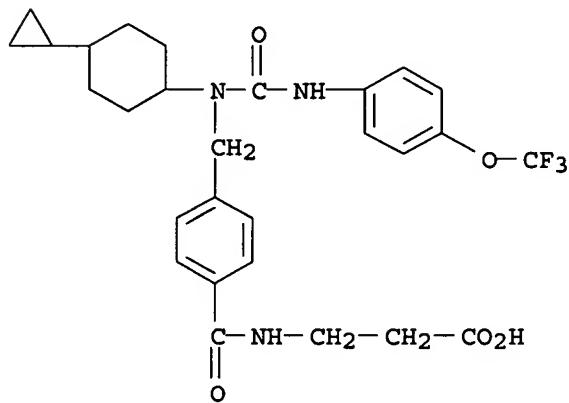
RN 307984-85-6 CAPLUS

CN  $\beta$ -Alanine, N-[4-[(4-cyclohexylphenyl)[[(3,5-dichlorophenyl)amino]carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)

RN 307984-86-7 CAPLUS

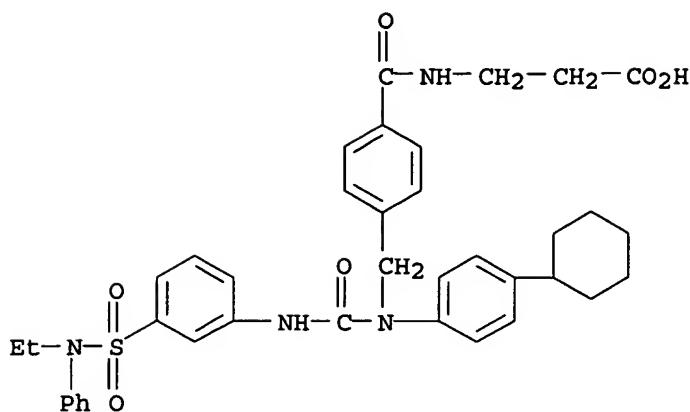
CN  $\beta$ -Alanine, N-[4-[[[(4-cyclohexylphenyl) [[4-[(trifluoromethyl)thio]phenyl]amino]carbonyl]amino]methyl]benzoyl]- (9CI)  
(CA INDEX NAME)

RN 307985-00-8 CAPLUS

CN  $\beta$ -Alanine, N-[4-[[[(4-cyclopropylcyclohexyl) [[4-[(trifluoromethoxy)phenyl]amino]carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)

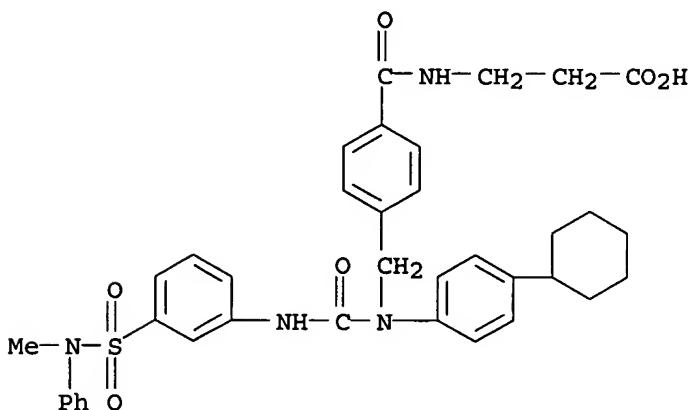
RN 307985-16-6 CAPLUS

CN  $\beta$ -Alanine, N-[4-[[[(4-cyclohexylphenyl) [[3-[(ethylphenylamino)sulfonyl]phenyl]amino]carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)



RN 307985-74-6 CAPLUS

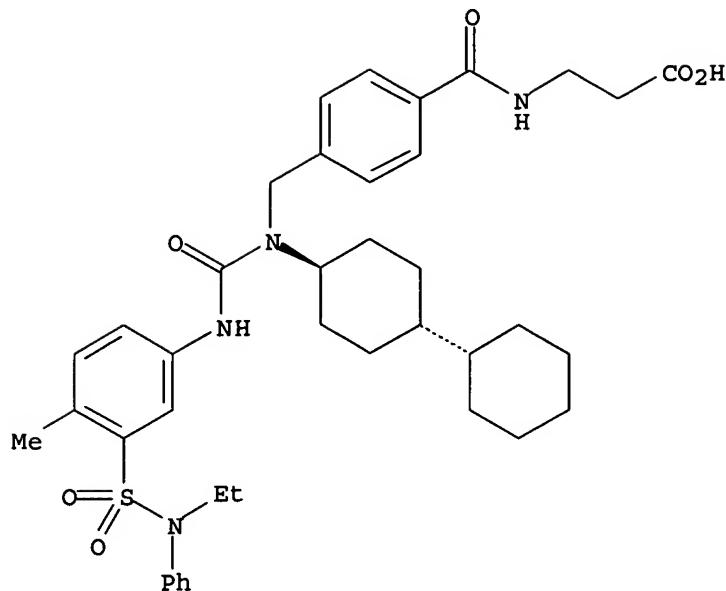
CN  $\beta$ -Alanine, N-[4-[(4-cyclohexylphenyl)[[[3-[(methylphenylamino)sulfonyl]phenyl]amino]carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)



RN 307986-43-2 CAPLUS

CN  $\beta$ -Alanine, N-[4-[[trans-[1,1'-bicyclohexyl]-4-yl][[[3-[(ethylphenylamino)sulfonyl]-4-methylphenyl]amino]carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)

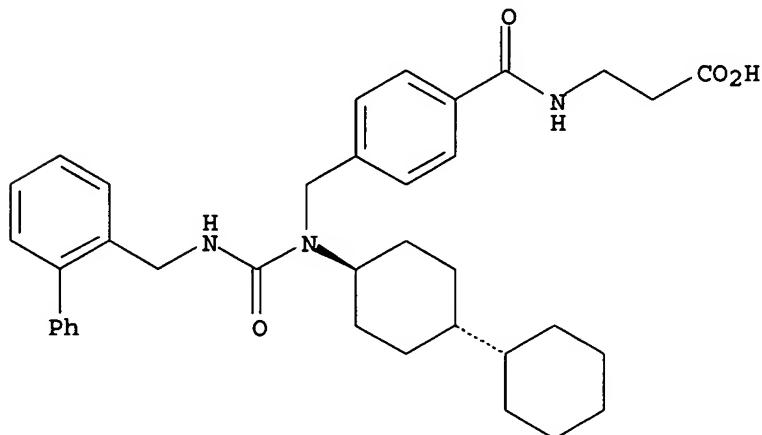
Relative stereochemistry.



RN 307986-44-3 CAPLUS

CN  $\beta$ -Alanine, N-[4-[[trans-[1,1'-bicyclohexyl]-4-yl[{{([1,1'-biphenyl]-2-ylmethyl)amino}carbonyl]amino}methyl]benzoyl]- (9CI) (CA INDEX NAME)

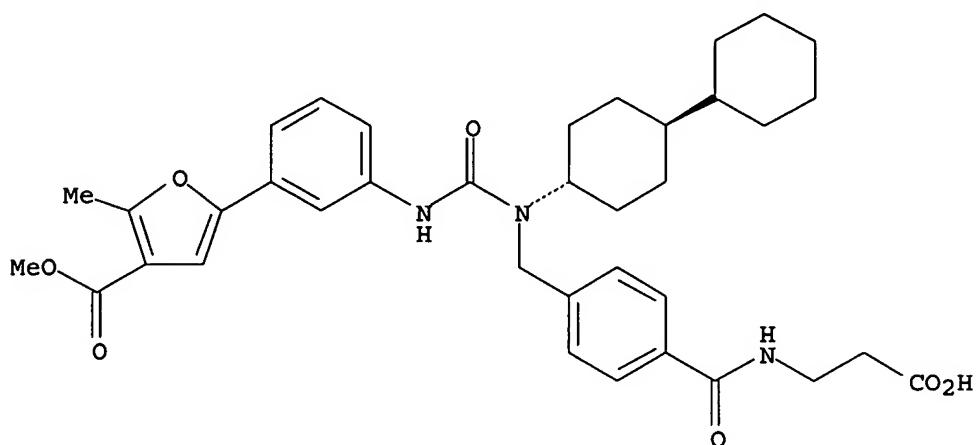
Relative stereochemistry.



RN 307986-45-4 CAPLUS

CN 3-Furancarboxylic acid, 5-[3-[[[trans-[1,1'-bicyclohexyl]-4-yl[{{[4-[(2-carboxyethyl)amino}carbonyl]phenyl}methyl]amino}carbonyl]amino]phenyl]-2-methyl-, 3-methyl ester (9CI) (CA INDEX NAME)

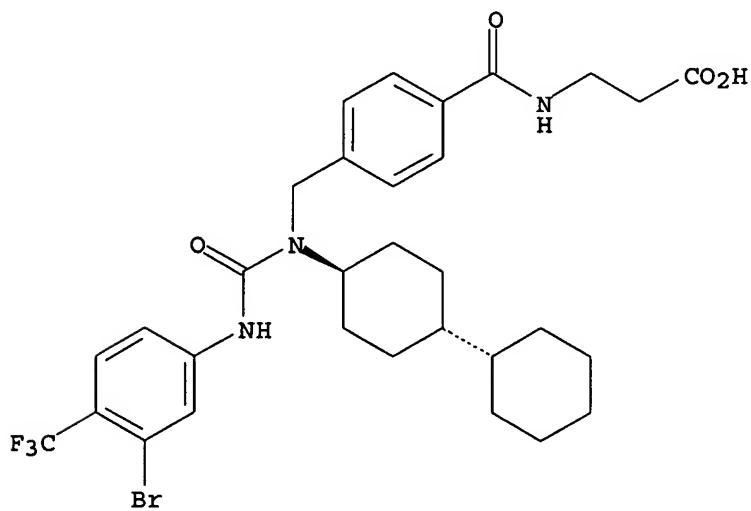
Relative stereochemistry.



RN 307986-46-5 CAPLUS

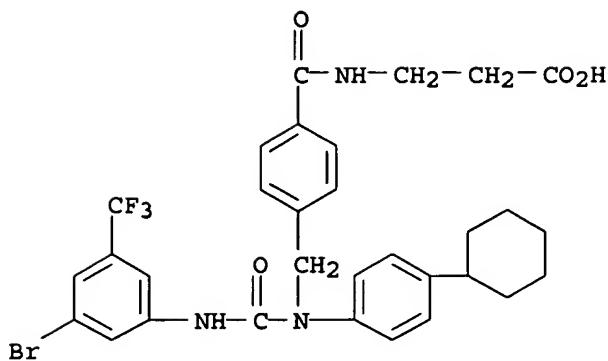
CN  $\beta$ -Alanine, N-[4-[[trans-[1,1'-bicyclohexyl]-4-yl][[3-bromo-4-(trifluoromethyl)phenyl]amino]carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



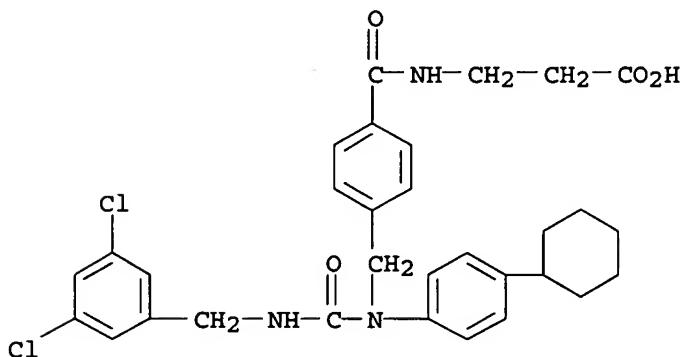
RN 307986-47-6 CAPLUS

CN  $\beta$ -Alanine, N-[4-[[[[[3-bromo-5-(trifluoromethyl)phenyl]amino]carbonyl](4-cyclohexylphenyl)amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)



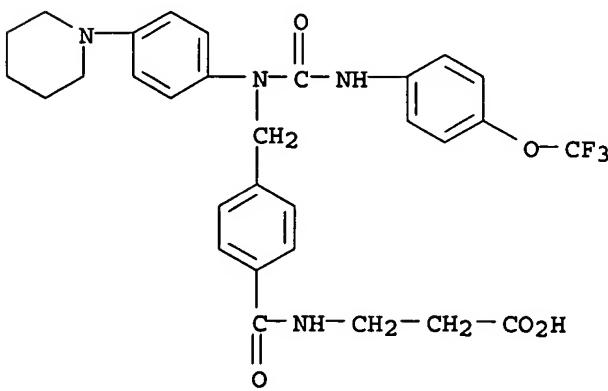
RN 307986-48-7 CAPLUS

CN  $\beta$ -Alanine, N-[4-[[[4-cyclohexylphenyl][[[(3,5-dichlorophenyl)methyl]amino]carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)

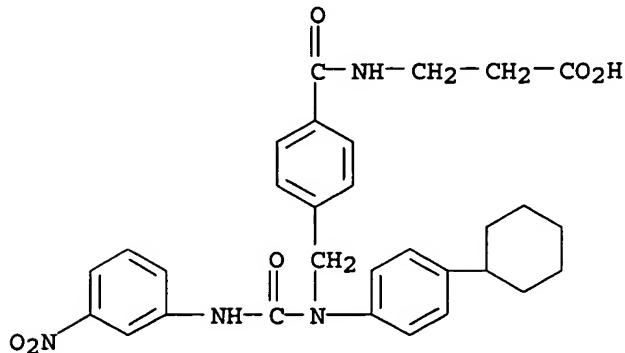


RN 307986-88-5 CAPLUS

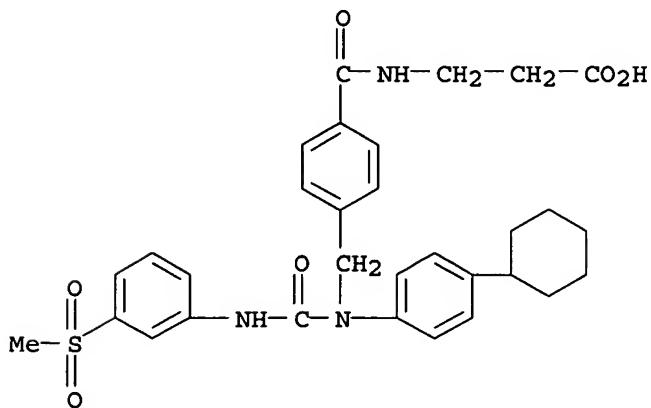
CN  $\beta$ -Alanine, N-[4-[[[4-(1-piperidinyl)phenyl][[[4-(trifluoromethoxy)phenyl]amino]carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)



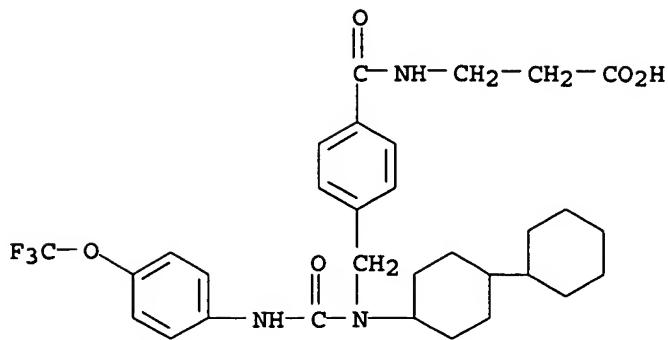
RN 307986-97-6 CAPLUS  
 CN  $\beta$ -Alanine, N-[4-[(4-cyclohexylphenyl) [(3-nitrophenyl)amino]carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)



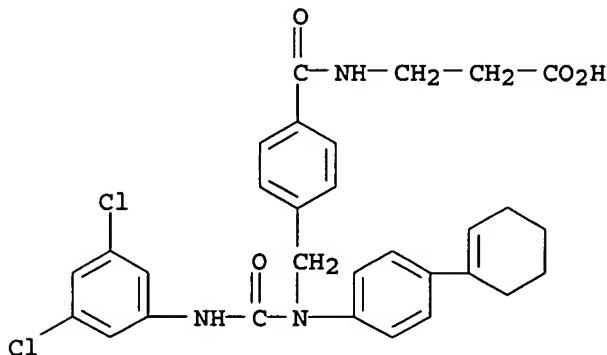
RN 307987-25-3 CAPLUS  
 CN  $\beta$ -Alanine, N-[4-[(4-cyclohexylphenyl) [[3-(methylsulfonyl)phenyl]amino]carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)



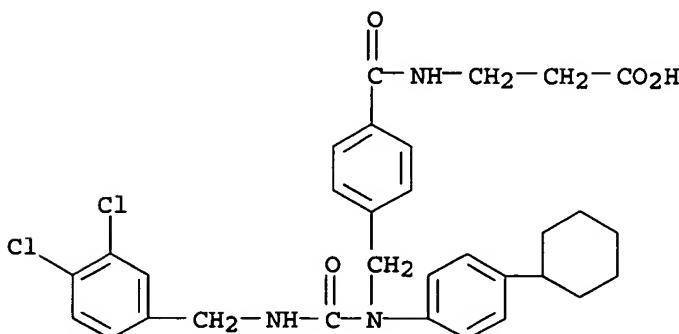
RN 307988-28-9 CAPLUS  
 CN  $\beta$ -Alanine, N-[4-[[[1,1'-bicyclohexyl]-4-yl[[[4-(trifluoromethoxy)phenyl]amino]carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)



RN 307988-56-3 CAPLUS

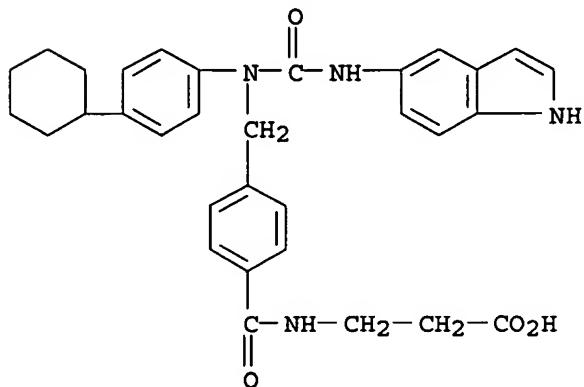
CN  $\beta$ -Alanine, N-[4-[[[4-(1-cyclohexen-1-yl)phenyl][[[(3,5-dichlorophenyl)amino]carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)

RN 307988-57-4 CAPLUS

CN  $\beta$ -Alanine, N-[4-[[[4-cyclohexylphenyl][[[(3,4-dichlorophenyl)methyl]amino]carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)

RN 307988-58-5 CAPLUS

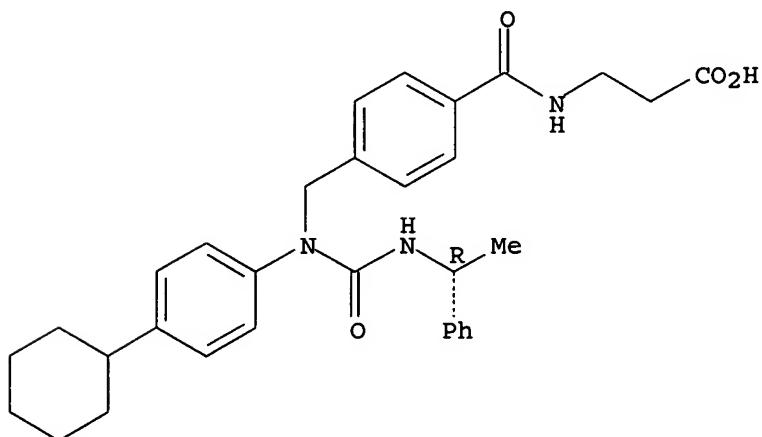
CN  $\beta$ -Alanine, N-[4-[[[(4-cyclohexylphenyl)[(1H-indol-5-ylamino)carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)



RN 307988-59-6 CAPLUS

CN  $\beta$ -Alanine, N-[4-[[[(4-cyclohexylphenyl)[[(1R)-1-phenylethyl]amino]carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)

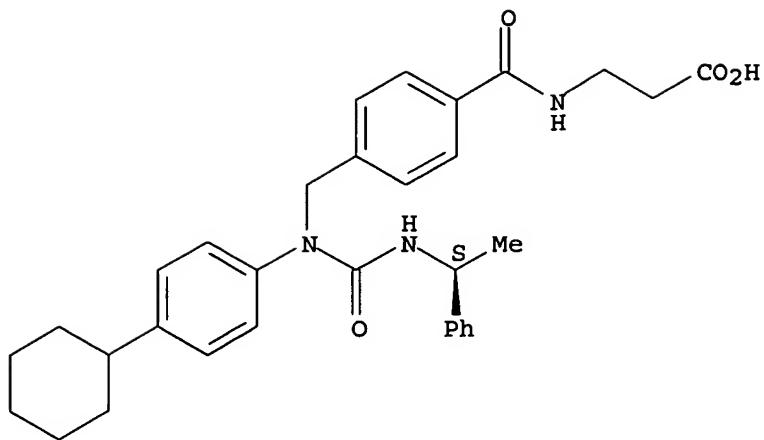
Absolute stereochemistry.



RN 307988-60-9 CAPLUS

CN  $\beta$ -Alanine, N-[4-[[[(4-cyclohexylphenyl)[[(1S)-1-phenylethyl]amino]carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)

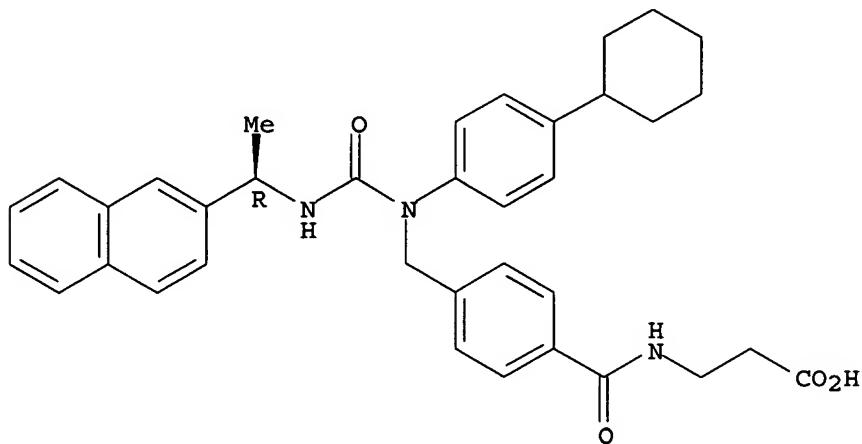
Absolute stereochemistry.



RN 307988-61-0 CAPLUS

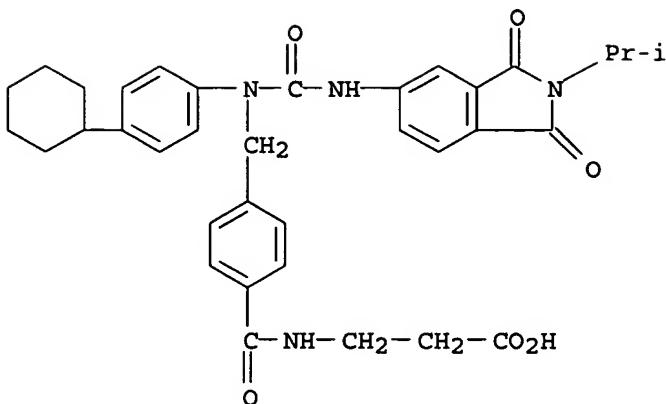
CN  $\beta$ -Alanine, N-[4-[(4-cyclohexylphenyl) [[[(1R)-1-(2-naphthalenyl)ethyl]amino]carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



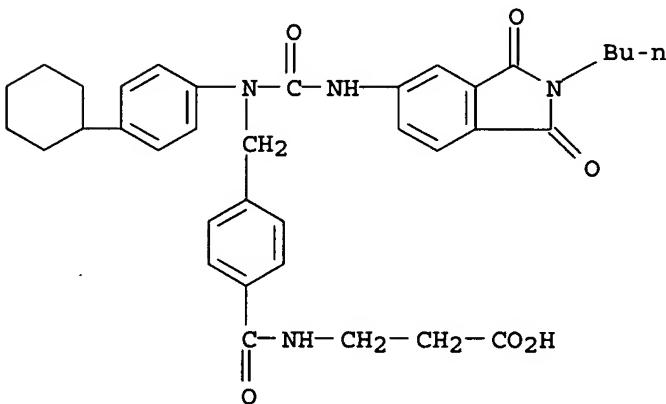
RN 307988-82-5 CAPLUS

CN  $\beta$ -Alanine, N-[4-[(4-cyclohexylphenyl) [[2,3-dihydro-2-(1-methylethyl)-1,3-dioxo-1H-isoindol-5-yl]amino]carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)



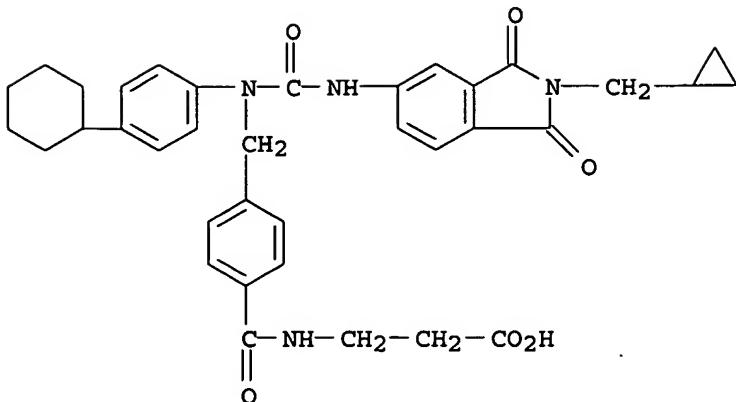
RN 307988-85-8 CAPLUS

CN  $\beta$ -Alanine, N-[4-[[[[(2-butyl-2,3-dihydro-1,3-dioxo-1H-isoindol-5-yl)amino]carbonyl](4-cyclohexylphenyl)amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)



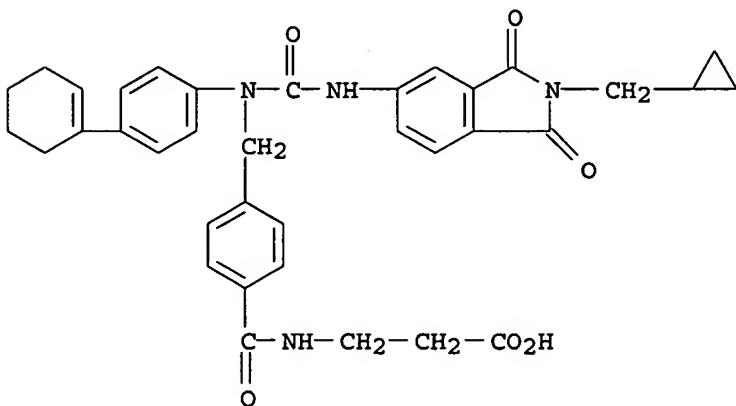
RN 307988-92-7 CAPLUS

CN  $\beta$ -Alanine, N-[4-[[[4-cyclohexylphenyl)[[2-(cyclopropylmethyl)-2,3-dihydro-1,3-dioxo-1H-isoindol-5-yl]amino]carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)



RN 307988-95-0 CAPLUS

CN  $\beta$ -Alanine, N-[4-[[[4-(1-cyclohexen-1-yl)phenyl] [[2-(cyclopropylmethyl)-2,3-dihydro-1,3-dioxo-1H-isoindol-5-yl]amino]carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)



IT 307984-31-2 307984-32-3 307984-33-4

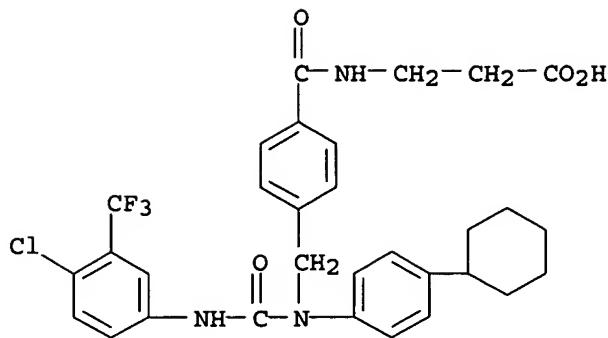
307984-34-5 307984-55-0

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of 3-(benzoylamino)propionic acid derivs. as glucagon antagonists/inverse agonists)

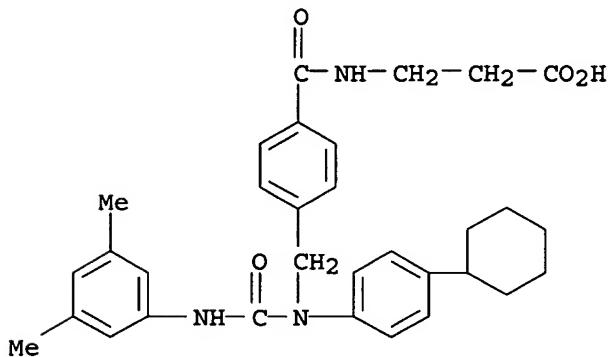
RN 307984-31-2 CAPLUS

CN  $\beta$ -Alanine, N-[4-[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl] (4-cyclohexylphenyl)amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)



RN 307984-32-3 CAPLUS

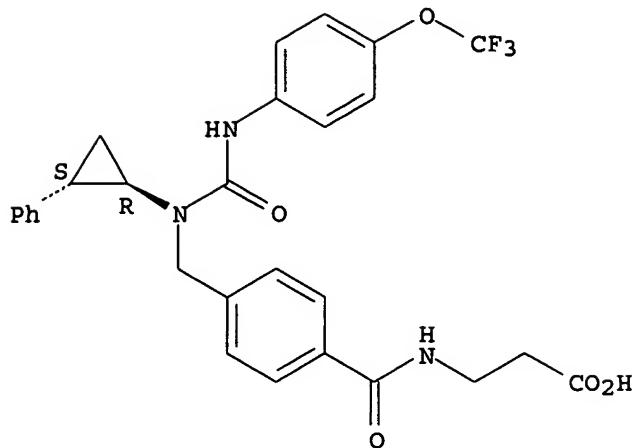
CN β-Alanine, N-[4-[(4-(3,5-dimethylphenyl)amino)carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)



RN 307984-33-4 CAPLUS

CN β-Alanine, N-[4-[[[(1R,2S)-2-phenylcyclopropyl][[[4-(trifluoromethoxy)phenyl]amino]carbonyl]amino]methyl]benzoyl]-, rel- (9CI) (CA INDEX NAME)

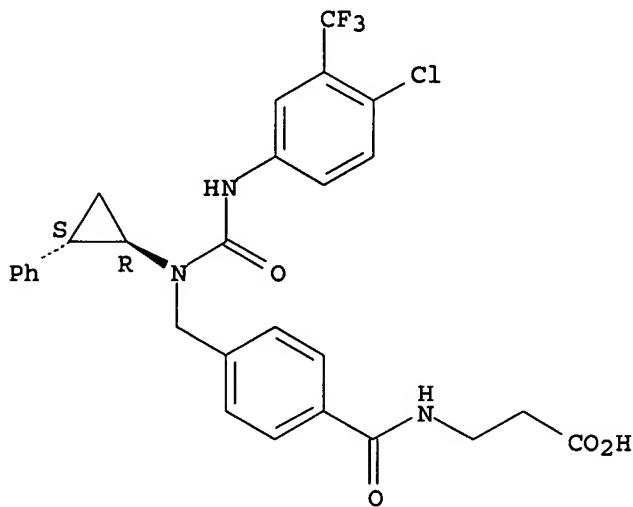
Relative stereochemistry.



RN 307984-34-5 CAPLUS

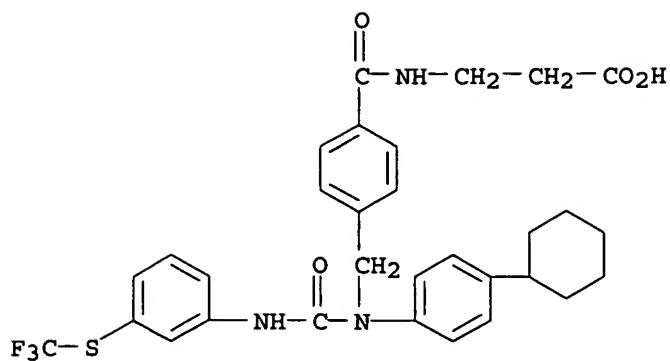
CN  $\beta$ -Alanine, N-[4-[[[[[4-chloro-3-(trifluoromethyl)phenyl]amino]carbonyl]((1R,2S)-2-phenylcyclopropyl)amino]methyl]benzoyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 307984-55-0 CAPLUS

CN  $\beta$ -Alanine, N-[4-[(4-cyclohexylphenyl)[[[3-[(trifluoromethyl)thio]phenyl]amino]carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT